Section: Obstetrics and Gynaecology

Original Research Article

CLINICOPATHOLOGICAL STUDY OF ABNORMAL UTERINE BLEEDING IN PERI-MENOPAUSAL AND POST-MENOPAUSAL WOMEN

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ABSTRACT

Background: AUB is the commonest menstrual problem, affecting 14-25% of women of reproductive age group and 50% during perimenopausal period. The study was conducted to determine the clinical and pathological profile of perimenopausal women presenting to Gynecology OPD, Government Medical College, Kollam with abnormal uterine bleeding.

Materials and Methods: The cross-sectional study was done in a tertiary care hospital in south Kerala for 6 months. 300 perimenopausal women (40 years and above till 1 year beyond menopause) who presented to Gynecology OPD at GMC, Kollam with abnormal uterine bleeding were included in the study. A standardized pretested proforma was used for data collection. Categorization of cases were done as per PALM-COEIN classification clinically and histopathologically and correlation was noted.

Results: Heavy menstrual bleeding was the most common menstrual complaint present in 43% cases. Hypertension was the commonest medical disorder associated with AUB (18.6%). On clinical classification, structural causes (PALM) contributed to 63% cases and functional causes (COEIN) constituted 37% cases, whereas PALM component contributed for 73% cases after histopathology. Proliferative endometrium was the commonest endometrial pathology (38.1%) followed by secretory endometrium (34.5%). On clinicopathological correlation there was statistically significant difference between clinical and histopathological diagnosis in AUB-A, AUB-A;L and AUB-E.

Conclusion: Advantages of PALM-COEIN is that it is an easy pneumonic and is globally applicable and provides standardized terminology for easier communication, effective management, and prognostication. In our study it is found that clinical and histopathological diagnosis are complementary, and optimization of treatment is achieved by allocation into a proper category.

Keywords: Perimenopausal, Abnormal Uterine Bleeding, Clinicopathological Study.

INTRODUCTION

Menstruation is the cyclical uterine bleeding occurring during the reproductive age group between menarche to menopause. Menstrual cycle is said to be within normal limits if cycle length is in the range of 24 to 38 days for 4.5-8 days with amount of menstrual blood loss ranging from 5-80ml1. Abnormal uterine bleeding (AUB) is the overarching term used to describe any departure from normal menstruation or from a normal menstrual cycle pattern.

The key characteristics of uterine bleeding are regularity, frequency, heaviness of flow, and duration of flow, but each of these may exhibit considerable variability. In AUB there are disturbances in regularity (irregular menstrual bleeding and amenorrhoea), disturbances of frequency(infrequent menstrual bleeding and frequent menstrual bleeding),disturbances of heaviness of flow(heavy menstrual bleeding and heavy and prolonged menstrual bleeding), disturbances in duration of bleeding (prolonged menstrual and shortened

menstrual bleeding),irregular non-menstrual bleeding and post-menopausal bleeding.[1]

Rationale of Study

AUB is the commonest menstrual problem, affecting 14-25% of women of reproductive age group and 50% during perimenopausal period.[2] It is a major cause of hysterectomy and significantly impacts the quality of life of women. There was general inconsistency in the nomenclature used to describe abnormal uterine bleeding (AUB), in addition to a plethora of potential causes,several of which may coexist in a given individual.[3] To solve this problem, FIGO (2011) approved a new classification system PALM –COEIN for causes of AUB in non-gravid women of reproductive age group. The classification was designed to create a practical system that could be used by clinicians in most countries worldwide to classify patients with AUB readily and consistently, based on the results of a systematic evaluation. There are 9 main categories, which are arranged according to the acronym PALM-COEIN (pronounced "palm-koin"): polyp; adenomyosis; leiomyoma; malignancy and hyperplasia; coagulopathy; ovulatory dysfunction; endometrial; iatrogenic; and not yet classified. In general, the components of the PALM group are discrete (structural) entities that can be measured visually with imaging techniques and/or histopathology, whereas the COEIN group is related to entities that are not defined by imaging or histopathology (non-structural).[3]

Endometrial tissue testing is recommended by FIGO as a first line management in women of perimenopausal age group with AUB. It has double advantage of detecting an accurate cause of bleeding as well as to rule out potential malignancies. Clinical and histopathological correlation is mandatory as redistribution of category can occur after histopathological correlation and also helps in standardization of treatment.

Objectives

1. To determine the clinicopathological profile of perimenopausal women presenting to Gynecology OPD, GMC KOLLAM with abnormal uterine bleeding
2. To categorize the causes of AUB in perimenopausal women under PALM-COEIN classification.
3. To establish clinicopathological correlation of various categories of AUB.

MATERIALS AND METHODS

Study Design: Cross sectional study.

Study Setting: Dept of Obstetrics and Gynecology, GMC, Kollam.

Study subjects.

Inclusion Criteria

Perimenopausal women (40 years and above till 1 year beyond menopause) who present to Gynecology OPD at GMC, Kollam with abnormal uterine bleeding and who give consent for the study.

Exclusion Criteria

Pregnancy, patient not giving consent for the study

Sample Size

300 cases attending the Gynecology OPD with abnormal uterine bleeding from January 2020 to June 2020. Sample size calculated by taking prevalence of leiomyomas (36%) and ovulatory disorders (25%)4 which were the most frequent causes of AUB according to other researchers using the formula 4pq by square of d (where p is the prevalence, q is (100-p) and d is 20% of p.

Materials & Method

The study included total 300 perimenopausal women with complaints of abnormal uterine bleeding (AUB), attending the department of Obstetrics and Gynecology at Government Medical college Kollam for 6 months from January 2020 to June 2020.

Data was collected in a pretested proforma. Demographic details, menstrual pattern, details of abnormal uterine bleeding, history suggestive of anemia, blood transfusion, previous surgeries, medical history, contraceptive history, drug history, history suggestive of coagulation disorders followed by general, systemic and gynecological examination was done .Complete blood count , thyroid function tests, liver function test and coagulation profile done according to the patient profile. Pelvic ultrasound was done to detect leiomyoma, adenomyosis and endometrial polyps and to assess endometrial thickness.

Initially clinical categorization of cases were done as per PALM-COEIN classification. Patients with polyp, adenomyosis, and leiomyoma after clinical examination and ultrasonography were categorized as AUB-P, AUB-A, and AUB-L respectively. Women with thickened endometrium and those with features of endometrial malignancy in ultrasound were classified under AUB-M. Patients on anticoagulants or with coagulation disorders grouped under AUB-C and referred to hematology for further evaluation. Cases were designated as AUB-O based on variable amount of bleeding and unpredictable timing after excluding other causes. Predictable or cyclical pattern of bleeding was designated as AUB-E . Steroid hormone intake during previous 3 months or abnormal bleeding following use of contraception was classified under AUB- I. The others not fitting in any category were included in Not yet classified category (AUB-N). Endometrial sampling was done with EZ VAC endometrial sampler in patients with thickened endometrium (>12mm) and in patients with ultrasound features suggestive of malignancy. Endometrial sampling was also done in patients with risk factors of endometrial hyperplasia and malignancy like obesity, diabetes, hypertension ,chronic anovulation as in polycystic ovarian syndrome ,family history of malignancies and patients with persistent, irregular and heavy bleeding irrespective of thin endometrium. Fractional curettage was done in patients who had inadequate tissue sample with EZ-VAC. Endometrial sampling, fractional curettage and hysterectomy specimens

were obtained and reallocation of categories were done after histopathological evaluation. Clinical diagnosis was correlated with histopathology based final diagnosis.

Statistical Methods

SPSS version 16 was used for data analysis and descriptive statistics presented as frequencies and percentages. Z- test was done to know the significance of correlation and $p<0.05$ was considered to be statistically significant.

RESULTS

The study included 300 women in perimenopausal age group .82% women belonged to 40- 50 year age group.70% women belonged to parity two or more. Heavy menstrual bleeding was the most common menstrual complaint present in 43% cases.

Table 1: Distribution of cases based on menstrual symptoms

PRESENTING COMPLAINT	NUMBER	PERCENTAGE
Irregular menstrual bleeding	24	8
Amenorrhoea followed by heavy menstrual bleeding	46	15.33
Frequent menstrual bleeding	30	10
Heavy menstrual bleeding	130	43.33
Heavy and prolonged menstrual bleeding	25	8.33
Prolonged menstrual bleeding	30	10
Intermenstrual bleeding	15	5

Dysmenorrhea was present in 31% women and majority had congestive dysmenorrhea. (70%). 6.2% women had severe anemia requiring blood transfusion. One case of idiopathic thrombocytopenic purpura was found in the study .2% women had irregular hormonal therapy leading to abnormal uterine bleeding. No case of IUCD related bleeding was there.

Hypertension was the commonest medical disorder associated with AUB (18.6%), followed by thyroid disorders (12%) and diabetes mellitus (7.3%) .8.6% women were obese (BMI >30). 3.3% had polycystic ovarian disease.

Table 2: Distribution of associated risk factors

RISK FACTORS	NUMBER	PERCENTAGE
Thyroid disorder	36	12
Hypertension	56	18.6
Diabetes mellitus	22	7.3
Obesity	26	8.6
PCOS	10	3.3

On clinical classification, structural causes (PALM) contributed to 63% cases and functional causes (COEIN) constituted 37% cases. Of the structural causes AUB- L was the major contributor (32.3%) followed by AUB-M (13.3%). Among functional causes commonest was ovulatory disorders (20%) followed by endometrial causes (15.3%). Dual pathology was detected in some cases - 3 cases of AUB-P;A, 6 cases of AUB-A;L and 2 cases of AUB-A;L;M were noted.

Table 3: Distribution of cases as per clinical diagnosis

DIAGNOSIS	TOTAL CASES	PERCENTAGE
PALM	189	63
AUB-P	21	7
AUB-A	20	6.6
AUB-L	97	32.3
AUB-M	40	13.3
AUB-P;A	3	1
AUB-A;L	6	2
AUB-A;L;M	2	0.66
COEIN	111	37
AUB-C	1	0.33
AUB-O	60	20
AUB-E	46	15.3
AUB-I	4	1.33
AUB-N	0	0

Histopathology was done for 220 cases, of which 120 were endometrial samplings, 95 hysterectomy specimens, and 5 endometrial curettings.

Proliferative endometrium was the commonest endometrial pathology (38.1%) followed by secretory endometrium (34.5%). Simple hyperplasia

without atypia was the most common hyperplasia on histopathology (9.54%). 4 cases of endometrial carcinoma were detected. .4 more cases of endometrial polyps were diagnosed after histopathology. Histopathology detected 20 more cases of adenomyosis compared to clinical diagnosis. AUB-A;L constituted 5% of total cases with 9 more cases detected after histopathology.

Based on histopathology, PALM component accounted for 73.3 % cases. Histopathology detected 31 more structural causes when compared to clinical diagnosis. In case of AUB-A and AUB-A;L ,more number of cases were detected by histopathology and the difference was statistically significant .In case of AUB-O and AUB- E histopathological findings reduced the number of cases detected clinically.

Table 4: Distribution of cases based on endometrial pattern on histopathology

HISTOLOGY OF ENDOMETRIUM	NUMBER(Total- 220)	PERCENTAGE
Proliferative	84	38.1
Secretory	76	34.5
Disordered proliferative endometrium	26	11.8
Simple hyperplasia without atypia	21	9.54
Simple hyperplasia with atypia	4	1.81
Complex hyperplasia	5	2.27
Complex hyperplasia with atypia	0	0
Chronic endometritis	0	0
Endometrioid carcinoma	4	1.81

Table 5: Distribution of cases after histopathology – based diagnosis

DIAGNOSIS	TOTAL	PERCENTAGE.
PALM	**220**	**73.3**
AUB-P	25	8.33
AUB-A	40	13.3
AUB-L	85	28.3
AUB-M	45	15
AUB- P;A	3	1
AUB-A;L	20	6.6
AUB-A;L;M	2	0.66
COEIN	**80**	**26.6**
AUB-C	1	0.33
AUB-O	50	16.6
AUB-E	25	8.3
AUB-I	4	1.33
AUB-N	0	0

DISCUSSION

Of the 300 women in my study ,82% belonged to 40-50 year age group and 43% had heavy menstrual bleeding as presenting complaint, similar findings were noted by Singh K et al and Mishra D et al. Amenorrhoea followed by heavy menstrual bleeding was the second most common menstrual complaint. This may be due to the unpredictable and irregular pattern of bleeding associated with perimenopause resulting from chronic anovulation. Hypertension, thyroid disorders, obesity, and diabetes were the most prevalent risk factors. In obese women there is peripheral aromatization of adrenal androgens to oestrogen which leads to leiomyoma, endometrial hyperplasia, abnormal uterine bleeding, and endometrial carcinoma.7

On clinical assignment, PALM and COEIN components constituted 63% and 37% respectively which changed after histopathological diagnosis to 73.3% and 26.6% respectively. Studies by other researchers showed equal distribution of PALM and COEIN components on clinical assignment, however significantly more cases of PALM component were revealed on histopathology similar to our study. Leiomyomas and ovulatory disorders were the most common causes of AUB in our study similar to studies by Qureshi F et al 8, Praveen.S et al9, Mishra D et al and Shankar et al10.

Histopathological examination was done in 220 cases and endometrial sampling was the most commonly practiced endometrial study technique in our study.

In AUB-P there was no significant difference in clinical and pathological diagnosis with only 4 additional cases detected by histopathology. This finding is similar to study by Mishra D et al and Singh K et al, but differs from findings by Malhotra et al11 and Khan et al12 where a significant difference was found between clinical and histopathological findings. This variation may be due to the fact that endometrial sampling was the most commonly employed technique in our study which may result in missing of endometrial polyps.

In AUB-A ,there was significant difference in clinical and histopathological diagnosis and the results were similar to studies by Mishra D,et al ,Singh K, and Khan et al .It may be because it is difficult to differentiate leiomyoma from adenomyosis clinically due to similar symptoms and signs. AUB-A was nearly doubled after histopathology and some cases of AUB-E were re-assigned as AUB-A after histopathology

14 more cases were assigned under AUB-A;L after histopathology which was statistically significant

.This observation was similar to findings by Mishra D et al ,Jetley et al13, Bhosle et al14, Khan.S et al, Mc-Pherson et al15 and Ramachandran et al16.

In AUB-L, there was no significant difference in clinical and histopathological diagnosis. This may be due to the ease of detection of fibroids by history, pelvic examination and ultrasound.

5 more cases of AUB-M were detected after histopathology with no statistically significant difference between clinical and pathological diagnosis, similar to studies by Archana Singh et al and Singh K, et al. This may be due to the fact that ultrasound detection of endometrial hyperplasia and malignancies have improved over time so that more number of cases can be detected prior to histopathology. This is in contrast to studies by Mishra D, et al.

In our study proliferative endometrium was the most common endometrial pathology followed by secretory endometrium, similar findings were noted by Jetley et al , Deka et al17 and Shukla .M et al18, but secretory endometrium was most common in studies by Mishra D,et al and Singh K,et al . Simple hyperplasia without atypia was the most common hyperplasia on endometrial study similar to findings by Singh K,et al and Prajapati R et al19 , Wahda et al20 ,Khare et al21 . Malignancy was found in 1.81%, similar findings were noted in studies by Kanika Singh, Inal zo et al22, Shukla et al and Deka et al.

In AUB-O, less number of cases were detected by histopathology, but the finding was not statistically significant. In AUB-O , diagnosis can be established from menstrual history alone in case of true anovulatory bleeding. Variable amount of irregular unpredictable bleeding with no clinically palpable abnormality of genital tract can be due to ovulatory disorder.

In AUB-E more number of cases were shifted to PALM component after histopathology which was statistically significant. AUB-E is generally a diagnosis of exclusion and is a primary disorder of endometrium and majority of cases are due to disturbances in prostaglandins, vasoactive mediators and tissue fibrinolytic activity and no sophisticated techniques are currently available to get a definitive diagnosis. Total number of AUB- E cases were reduced to half after histopathology.

Table 6: Correlation of clinical and histopathology based diagnosis

DIAGNOSIS	CLINICAL PALM n=189(63%)	HISTOPATHOLOGICAL PALM n=220(73.3%)	P value
AUB-P	7%	8.33%	>0.05(NS)
AUB-A	6.6%	13.3%	<0.05(S)
AUB-L	32.3%	28.3%	>0.05(NS)
AUB-M	13.3%	15%	>0.05(NS)
AUB-A;L	2%	6.6%	<0.05(S)
DIAGNOSIS	**CLINICAL COEIN n=111(37%)**	**HISTOPATHOLOGICAL COEIN n=80(26.6%)**	**P value**
AUB-O	20%	16.6%	>0.05(NS)
AUB-E	15.3%	8.3%	<0.05(S)

The drawback of PALM-COEIN system is that there is no sub categorization of malignancy and hyperplasia, and both are included in same group AUB- M.[23]

CONCLUSION

In the present study, PALM and COEIN components constituted 63% and 37% respectively on clinical assessment and 73.3% and 26.6% after histopathology. The difference was attributed to detection of more cases of AUB- A and AUB-A;L and reallocation of more number of AUB-E to structural component by histopathology. On clinicopathological correlation there was statistically significant difference between clinical and histopathological diagnosis in AUB-A, AUB-A;L and AUB-E .Advantages of PALM-COEIN system is that it is an easy pneumonic and it is globally applicable and provides a standardized universal terminology of easier communication, effective management and prognostication21In addition endometrial sampling is a cost effective , effective and simple method which can be used with more or less accurate diagnostic yield.

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